Future Directions in Engineering Biology

April 4 - 5, 2011
Berkeley, CA

Workshop Co-Chairs:

Adam Arkin | Douglas Clark | Matthew Tirrell
University of California, Berkeley

Sponsored by the
Department of Defense, Office of the Assistant Secretary of Defense
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UC BERKELEY SYNTHETIC BIOLOGY INSTITUTE

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I. Executive Summary

Biological Engineering is the application of engineering principles to the design, construction, and characterization of biological systems. A central goal is to make the engineering of biology and biomimetic systems faster and more predictable, and thus to enable all constructive biotechnologies. Key points made during this two-day workshop are:

1. There is a compelling need for new measurement technologies, and even more, for standardization, validation and organization of the vast amounts of biological data being generated. This is an opportunity for a large-scale effort dedicated to biological data management. Given the genomic data available, the challenge is to reconstruct biological network structures (genotype to phenotype modeling) from these data.
2. A general strategy for systems biotechnology to produce a diverse array of products (drugs and other therapies, fuels, chemicals and materials) is emerging, building on an iterative interplay between systems biology (high-throughput analysis and predictive model development) and synthetic biology (metabolic engineering according to some reliable methodologies), followed by larger-scale process optimization.
3. The major technical challenges in engineering biology are:

   (a) Understanding cellular networks (from genomic information) and hierarchical relationships, molecular to cell, organism, tissue. This is a challenge to data acquisition, modeling and design in biological engineering. Lack of scalable design strategies for reliable biological design retards the development of biological engineering.

   (b) Creating actual knowledge out of massive amounts of data; a need for data standardization and validation; a national lab-type effort for validation and accessible maintenance of large data bases required for modern biology would be invaluable.

   (c) New, more rapid tools for biological synthesis and characterization are needed. There is a lack of diversity and utility of existing biological parts. Biofabrication facilities are needed, akin to microelectronic integrated circuit fabrication facilities.
4. Modeling as a tool in biological engineering is a key to predictable, reliable biodesign. In biology-based systems most variables are unknown and very few of those known are controllable. Thus, construction and validation of models in biology is challenging. Modeling in biological engineering is more likely to be successful when it is data-driven, rather than theory- or intuition-driven.
5. Looking forward, we expect biological engineering to produce major advances in biomedicine (designer drugs and therapeutic systems, new biomimetic devices for high throughput drug testing, new agents to treat infectious diseases, stem cell therapies, understanding human biology) and biological manufacturing (bio-based production of fuels, chemicals, and materials, replacing fossil resources.) New capabilities in environmental sensing and remediation are also anticipated. In five years, expect new

biologically derived fuels to become more prevalent. Ten years will see biomanufacturing of high-value commodity chemicals, and on a slightly longer time-scale impacts on agriculture to increase yield, improve food supply and decrease negative environmental impacts. Over a decade, biological engineering will deliver more advanced solutions in health and medicine (e.g. genetically programmed regenerative medicine, or synthetic organs and tissues) and environmental remediation (e.g. rebuilding devastated environments and ecosystems).

6. The impacts of these advances will improve human health, sustainability, global health and nutrition, and security for the United States and the world.

II. Objectives of the Workshop

This gathering, organized by the UC Berkeley Department of Bioengineering and sponsored by the Office of the Assistant Secretary of Defense for Research and Engineering within the Department of Defense (DOD/ASD R&E), convened a group of approximately 25 thought leaders of the field to provide a perspective on potential breakthroughs and barriers to advancement in this growing and rapidly evolving field. While DOD interest was ultimately a factor in the discussions, the overall goal was to ensure that current scientific understanding at ASD(R&E) is informed by farsighted advice and expertise external to DOD. Topics covered by the invited speakers included, but were not limited to: Chemical Synthesis and Production; Therapeutic Organisms; Bio-Directed Materials Science and Nano-Science; Tissue Engineering; Agriculture Bioengineering; Environmental Bioengineering; Biological Systems Modeling; Computer-Aided Design; and Manufacturing with Biological Systems. During the workshop and in follow-up afterward, participants addressed major questions concerning: What are the major scientific challenges in engineering biology? What important advances might be made in the next 5-10 years and why they could be significant, in general, and for DOD, specifically? Where could future research efforts in biological engineering be most profitably focused? What could biological engineering do for DOD and the country in the next few decades? What are the barriers that can be foreseen to achieving these predictions of technological success?

III. Structure of the Workshop

The Workshop took place over two days and comprised 23 active participants from universities and industry, and 7 DOD research program directors. Over the two days, sessions consisted of five groups of four speakers with ten minutes discussion devoted to each individual talk, and one hour of general discussion after each session of four speakers. The workshop concluded with a 90-minute general discussion involving all participants. All materials presented are available to all participants in a password-protected website:

http://genomics.lbl.gov/dodmdiucb2011/

The program, with titles of sessions and individual talks, is provided as an appendix.

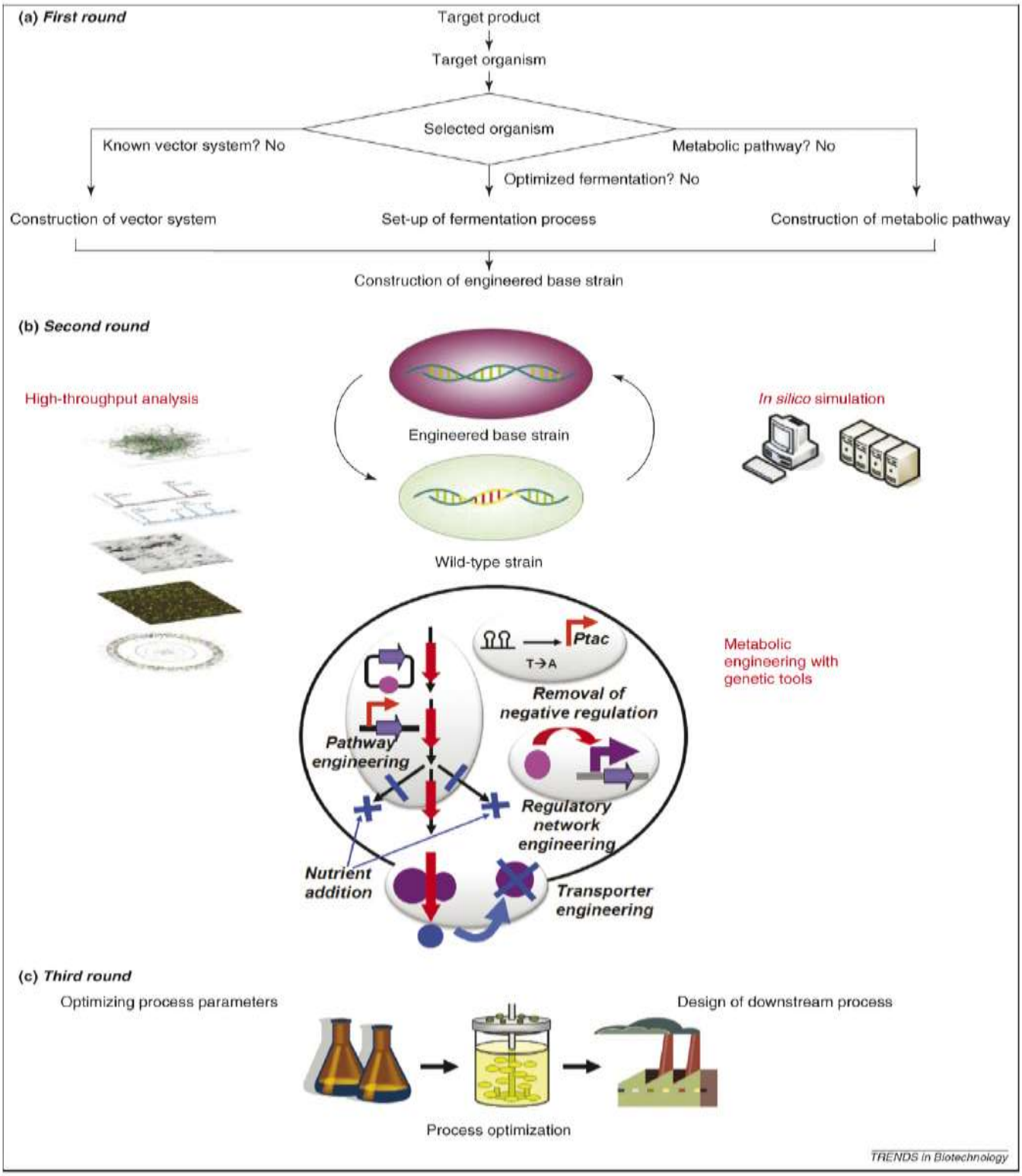
IV. Major Points from the Five Sessions

1. Chemical Synthesis and Production

The first session concentrated on routes to synthesis and large-scale manufacturing in biological organisms of a variety of products, including pharmaceuticals and other therapeutic agents, chemicals, fuels and materials. George Georgiou of the University of Texas discussed the discovery and development of the next generation of protein therapeutics, including enzymes to deplete metabolites as a cancer therapy and with a particular emphasis on anti-infective agents (antibiotics, anti-virals, vaccines, anti-fungals). The facts that such anti-infectives have well-understood and highly specific mechanisms of action, as well as favorable and well-defined safety and toxicology profiles, make them practical targets for development of commercial products. Georgiou advocates a "third-wave" approach to antibody discovery, employing tools such as nextgen sequencing to mine information on antibody production in bone marrow of a wide variety of species, as a means of accelerating the process.

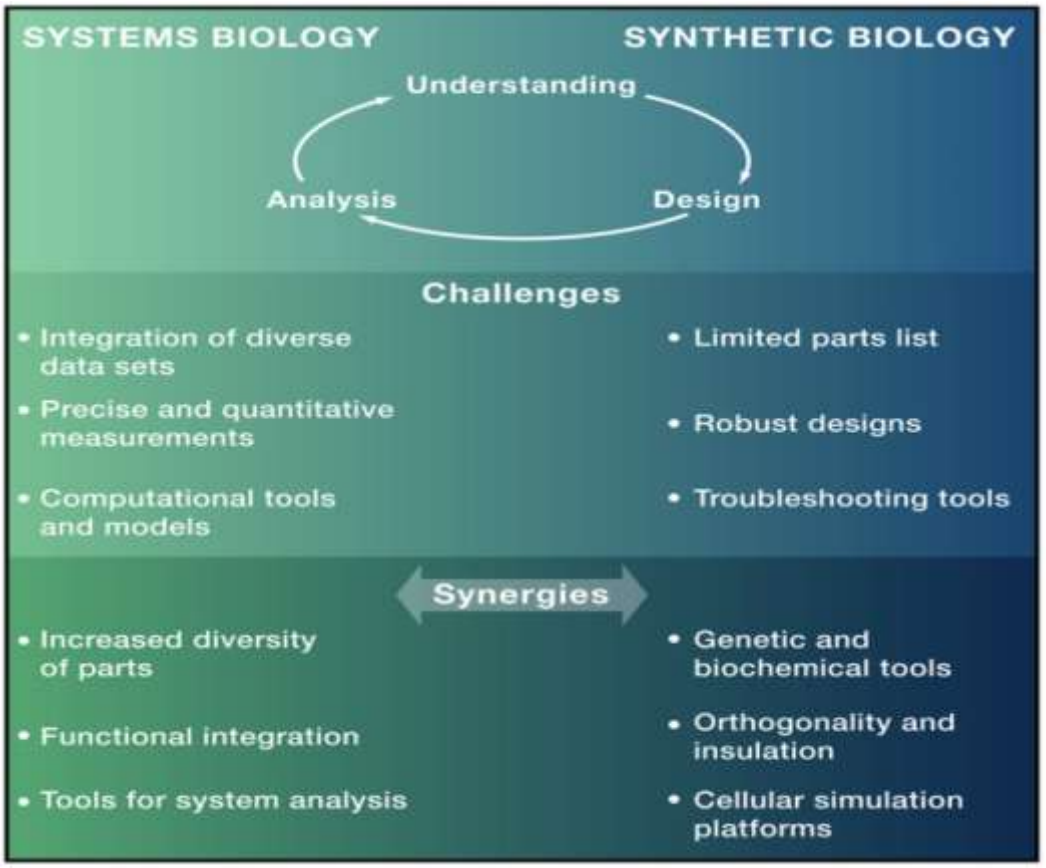
Sang Yup Lee of the Korea Advanced Institute of Science and Technology outlined a general strategy for systems biotechnology to produce a diverse array of products, illustrated schematically in the figure next page, taken from Park, S.J., Yang, T.H., Kang, H.O., Lee, S-H., Lee, E.J., Kim, T.W., Lee, S.Y., "Application of systems biology for bioprocess development", (2008) *Trends Biotechnol*., **26**, 404-412.

He points out a few dozen common polymers built from monomers that can be produced biologically. The figure (next page) illustrates the stages of process development that are leading to success in these efforts: selection of base strain; interactive phase of systems biology (high-throughput analysis and predictive model development) and synthetic biology (metabolic engineering according to some reliable methodologies); and process optimization. This iterative process development scheme is applicable to a wide range of desired products. (Barrett, C.L., Kim, T.Y., Kim, H.U., Palsson, B.Ø., and Lee, S.Y., "Systems biology as a foundation for genome-scale synthetic biology ", (2006) *Curr. Opin. Biotechnol.* **17**, 488-492.)


(a) First round
Target product
Target organism
Selected organism
Known vector system? No
Metabolic pathway? No
Optimized fermentation? No
Construction of vector system
Set-up of fermentation process
Construction of metabolic pathway
Construction of engineered base strain
(b) Second round
High-throughput analysis
Engineered base strain
Wild-type strain
In silico simulation
Ptac
T→A
Removal of negative regulation
Pathway engineering
Regulatory network engineering
Nutrient addition
Transporter engineering
Metabolic engineering with genetic tools
(c) Third round
Optimizing process parameters
Design of downstream process
Process optimization
TRENDS in Biotechnology

Willem Stemmer of Amunix, Inc. made the case for biological engineering by directed evolution. He demonstrated the effectiveness of directed evolution via the development of Amunix's XTEN technology, which prolongs the half-life in the blood of biomacromolecular therapeutics. He provided further examples of directed evolution in microbial communities, with application to wastewater treatment, and in non-biological polymers. Directed evolution is in a sense an alternative to synthetic biology, drawing on opportunities inherent in natural diversity more than on design.

Pamela Silver of Harvard University underscored the interaction between systems biology and synthetic biology, as illustrated in the figure below (taken from: Smolke, C.D., Silver, P.A., "Informing biological design by integration of systems and synthetic biology", (2011) *Cell* **18**, 855 859).



She showed that the naturally occurring carbon fixation organelles, carboxysomes, in some organisms could be engineered into other platform organisms, such as *E. coli*, leading to possibilities for widespread deployment. Additional examples of engineering organisms to produce hydrogen or to give rise to efficient photosynthesis were discussed.

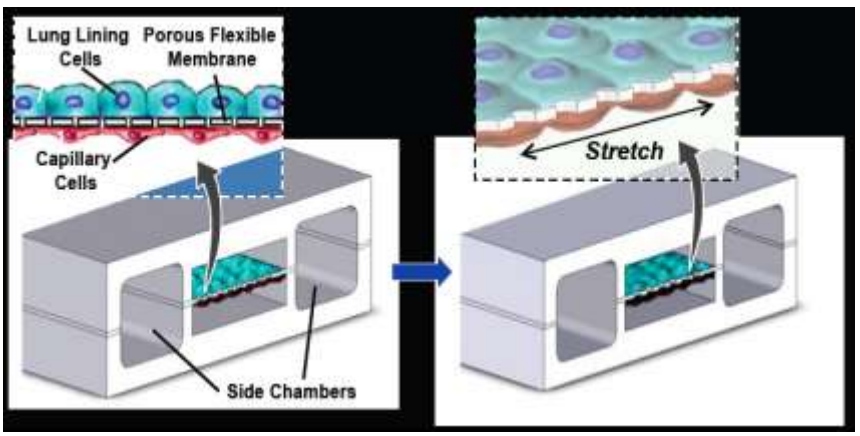
2. Biological Design and Assembly

Steve Laderman of Agilent Technologies discussed the role of bioanalytical measurements in the future of biological engineering. Dr. Laderman expressed the opinion, which is motivating Agilent's business strategy as a leading instrumentation manufacturer, that synthetic biology methods have the potential to significantly change manufacturing processes, research practices, and the associated measurements in all major industrial and biomedical market segments. Instrumentation companies see major opportunities in providing for the bioanalytical measurement needs of a biotechnology industry driven by synthetic biology.

Chris Voigt of the University of California, San Francisco (soon of the Massachusetts Institute of Technology) discussed the design and building of genomes from the bottom-up. This ambitious direction aims to eliminate the problems of native regulation, gain complete control over the desired function, facilitate further engineering and move toward the design of whole new genomes. This direction is fundamentally distinct from the directed evolution methodology of Pim Stemmer and Frances Arnold. In this approach, non-essential genes are eliminated, non-coding DNA is removed, codon usage is optimized, and operons are reorganized to produce synthetic biological parts, subject to synthetic biological control. Excellent DNA synthesis and assembly are essential tools in pursuing this direction. Voigt's team is achieving success in constructing nitrogen fixation capability via genome design.

Roy Curtiss of Arizona State University presented work on the genetic manipulation of vaccines. He has demonstrated the possibilities in this direction *via* development of recombinant *Salmonella* vaccine strains with regulated delayed attenuation and regulated delayed expression of codon-optimized genes encoding protective antigens that: grow more rapidly analogous to wild-type strains; colonize lymphoid tissues to a higher level; and induce better immune responses than vaccine strains without such regulated delays in attenuation and gene expression.

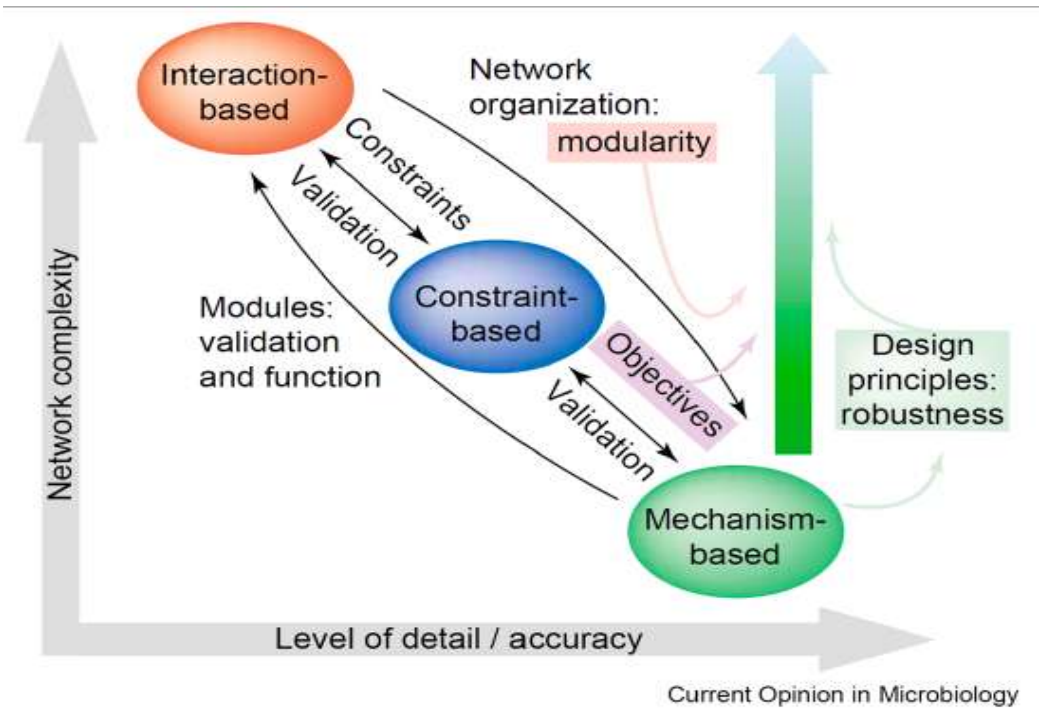
Donald Ingber of Harvard University discussed the biologically-inspired engineering of model organs. The goal of this direction is to engineer microchips or other model systems containing living cells that reconstitute human organ functions for drug screening, as well as diagnostic and therapeutic applications. The possibilities to accelerate drug development and replace animal testing by this means are attractive and realistic. A biomimetic spleen for sepsis therapy, a "breathing" lung-on-a-chip (see figure right) to examine pulmonary surfactants and other functional constituents, as well as toxic effects of nanoparticles, and a micro-heart-lung machine have been demonstrated.



3. Biological Systems Modeling.

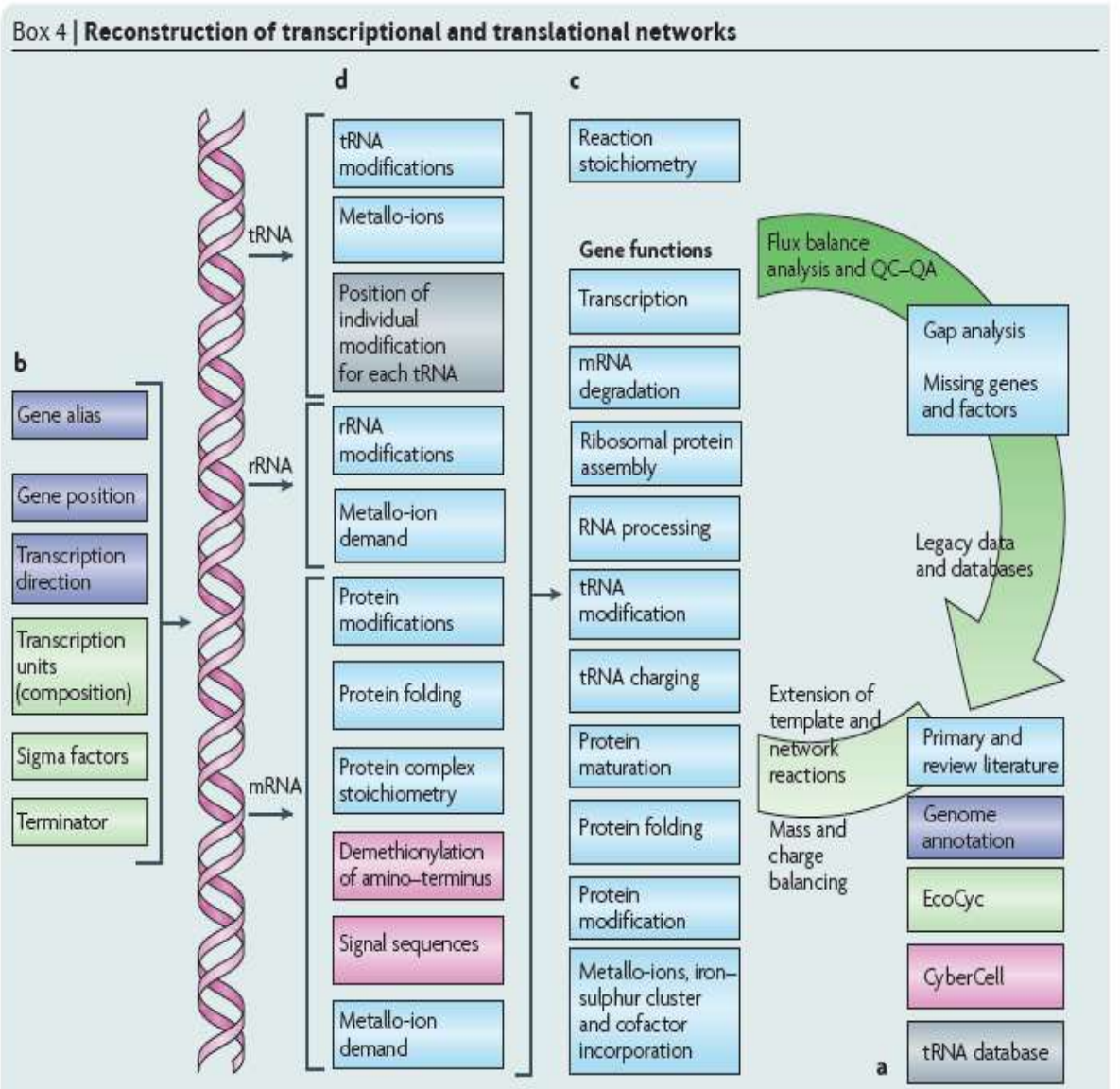
Douglas Lauffenburger of the Massachusetts Institute of Technology began his presentation with the following statement: "*At the present juncture, our capability for manipulating biology has far outpaced our capability for predicting what will happen when we do. Thus, it is highly problematic to: (a) undertake true design of a biological technology; (b) estimate cost-benefit ratio of a biological technology; and, (c) estimate risk-benefit ratio of a biological technology.*" He pointed out the fact that in most physical science-based systems, variables are usually known and controllable. Thus, construction and validation of models in physics and chemistry may be difficult but is straightforward, whereas in biology-based systems most variables are unknown and very few of those known are controllable. Thus, construction and validation of models in biology is highly – and rightfully – suspect. Modeling in biological engineering is more likely to be successful when it is data-driven, rather than theory- or intuition-driven. Perturbations (and resulting responses) are generally easier to produce than comprehensive experimental data so modeling is often based on negative data (lack of a sensitive response) rather than positive data. Lauffenburger demonstrated examples of top-down (from physiological to molecular), bottom-up (from "omic" data to physiological function) and middle-out (relating cell biology to molecular properties). All of these approaches require multi-scale modeling methods, in which modeling methods appropriate to different scales of size, time and behavior, must integrate and match seamlessly across scales.

Frank Doyle of the University of California, Santa Barbara discussed modeling strategies for drug targeting and biomarker discovery. He pointed out the necessary trade-offs between detailed accuracy and capturing complexity in biological modeling. See figure below, presented by Doyle taken from: Stelling, J., "Mathematical models in microbial systems biology", *Current Opinion in Microbiology*, (2004) **7**, 513-518.



Doyle discussed the problems of identifiability and parameter estimation in biological systems in some detail. He illustrated approaches to these issues in the context of biological models for type II diabetes and post-traumatic stress disorder.

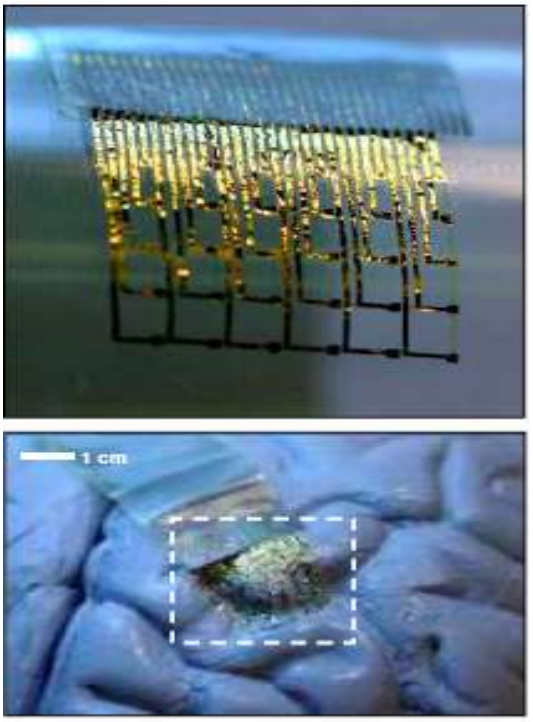
Bernhard Palsson of the University of California, San Diego gave a third perspective on biological systems modeling, as part of which he quoted Sydney Brenner: "*We are drowning in a sea of data and thirsting for knowledge. Most biology today is low-input, high-throughput, and no-output biology*." This perspective is that of microbial systems biology as genome-scale science, moving toward a mechanistic metabolic genotype-phenotype relationship in microbes. More simply put, since we are now in possession of many entire organismal genomes, the goal of modeling should and can be the reconstruction of biological networks from whole genome information, what Palsson terms synthetic biology on a genome scale. (See figure below) If this can be achieved, a goal of high-throughput, *in silico* biology will be realized, putting a mechanistic basis on the genotype-phenotype relationship.



Jay Keasling of the University of California, Berkeley continued the discussion of *Chemical Synthesis and Production*. He made a presentation entitled Synthetic Biology of Synthetic Chemistry, making similar points to those of Sang Yup Lee, about the enormous promise and versatility of synthetic biology as a manufacturing route to drugs, fuels and chemicals. Keasling reviewed the development from inception to commercialization of the anti-malarial, artemisinin. He pointed out that, though successful, this development was expensive and difficult to repeat owing to lack of systematic standardization in biological fabrication, arguing for the development of something akin to computer-aided design of microelectronic integrated circuits. "*Without standard parts and models, biological engineering is unpredictable*," he said. Keasling laid out the following set of challenges: Enzymes to catalyze all of the reactions we need; Genetic controllers for all of the genes (BioFab); Models adequate for design (BioCAD); Hosts that readily consume inexpensive substrates; Hosts that are tolerant of the target molecule.

4. Tissue Engineering and Biohybrid Systems

Linda Griffith of the Massachusetts Institute of Technology explored several issues in the biological engineering of tissue regeneration, that is, the process of combining cells with scaffolds to grow new tissues in patients. She discussed the question: What **molecular cues** (ligands) can we display on the scaffolds to elicit desired **cell responses**: *survival, growth, differentiation*? Effects of ligand density and spatial distribution are demonstrably important in the molecular design of materials to control cell behavior. Stem cells are increasingly important in tissue engineering, leading to a set of important questions concerning: Selection of progenitor cells from marrow; Survival of transplanted cells in the presence of possible hypoxia and inflammatory cytokines; Blood vessel in-growth; Proliferation and differentiation of cells, leading to remodeling into mature tissue. Griffith made the interesting point that engineered tissues may have important application as *in vitro* test beds for drug discovery and other trial therapies (in addition to tissue regeneration *in vivo*) in a similar manner to Ingber's organs-on-a-chip.



David Kaplan of Tufts University continued the discussion of biopolymer engineering for new materials and regenerative medicine. High performance ultra-lightweight protein material systems are his field, including biosynthetic elastins, silks, celluloses and collagens. Challenges in producing these materials are: high yields, pure proteins, high molecular weight, control of material properties, predictive models and tools. Kaplan showed interesting examples of biosynthetic silk as a substrate for flexible electronics and electrodes for brain stimulation (image right). Many applications, ranging from tissue engineering to robotics, are being explored for these versatile materials.

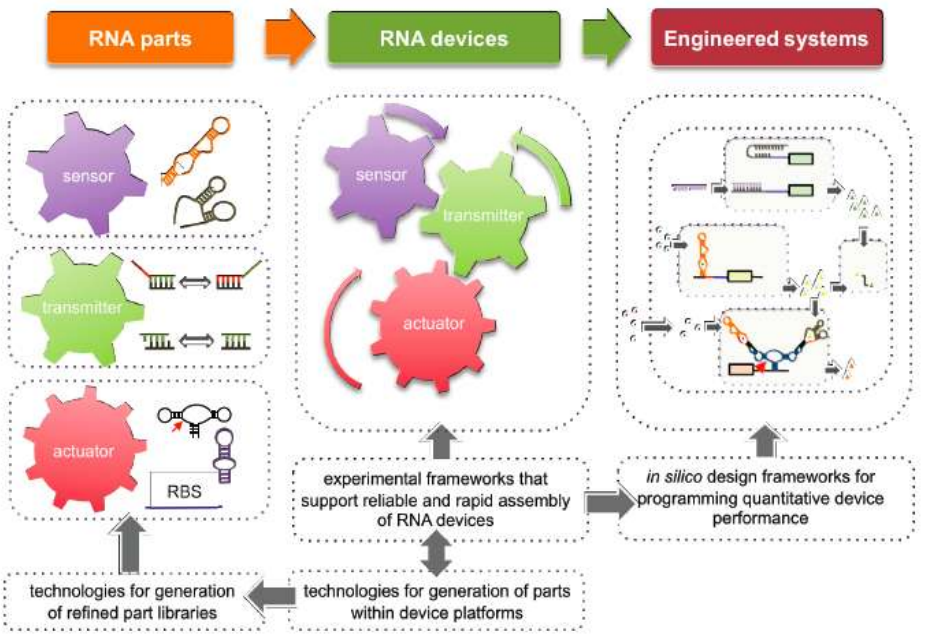
Niles Pierce of Caltech has developed the systematic design of small conditional RNAs that execute diverse dynamic functions. Small conditional RNAs (scRNAs) interact and change conformation to execute molecular logic *in vitro*, *in situ*, and *in vivo*. They are working to develop mathematically rigorous, physically sound, computationally efficient algorithms for programming molecular function. Current algorithms are available at nupack.org. The long-term goal is to develop a compiler for molecular programming that takes as input a modular conceptual device design and provides as output the sequences of scRNAs that interact to implement the desired function. They can engineer small conditional RNAs that function as conditional chemotherapies, selectively activating in diseased cells while leaving normal cells untouched, or that function as programmable molecular instruments within intact biological specimens.

5. Energy, Agriculture, Environment

Lisa Alvarez-Cohen of the University of California, Berkeley spoke about biodegradation of water contaminants. One aim of this work is to expand re-use of potable water as a means of conservation. Her group has characterized and optimized a strain of micro-organism, *Pseudonocardia dioxanivorans CB1190*, for dioxane biodegradation and is working on several other projects of this type. The role of biological engineering in bioremediation of water is clearly important.

Gary Sayler of the University of Tennessee addressed *inter alia* polycyclic aromatic hydro-carbons and identification of possible micro-organisms for their bioremediation. He described interesting biosensor and bioreporter applications in environmental sensing for bioremediation purposes. In this broad area of environmental applications, biological engineering brings tools, not only for remediation itself, but sensitive for analytical reporting on low-level contaminants.

Christina Smolke of Stanford University discussed synthetic genetic languages for probing and programming cells. She placed special emphasis on RNA-based tools and devices in synthetic biology, as illustrated in the figure from her talk below.



Win MN, Liang JC, Smolke CD. 2009. *Chem Biol.* 16: 298-310

Applications of these RNA devices have been made to gene silencing and splicing, and ribozyme cleavage. RNA can perform some important functions of proteins, without immunogenicity. Smolke's group has created synthetic T-cell regulatory networks for advanced cellular therapies and has developed molecular sensors, controllers and new discovery tools. Among the challenges she pointed out are the limited diversity of standard, reliable biological parts and the need for scalable, integrated design strategies.

Wendell Lim of the University of California, San Francisco described learning the design principles of cell signaling systems for the purposes of synthetic biology. He points out that the essence of biology is information processing and asks whether we are, or will be, able to engineering that. His focus is whether we can rewire the signal transduction networks of cells, that is, the networks of proteins that control rapid, spatial and temporal responses of cells. He asks, "Rather than understanding how any one particular circuit works, can we theoretically enumerate classes of solutions to common biological information processing problems?" – a profound question.

V. Major Points from the Concluding Discussion Session

Several applications of engineered biology brought out during this two-day workshop are potentially world-changing: biofuels, biomaterials, organisms that sequester carbon, new therapeutics, neuroscience applications, bio-hybrid robotics, clean water. Biology is in the lead in many, if not most, of the major problems facing society: energy, human healthcare, public and global health nutrition, agriculture, resource conservation, and clean water. These ideas were held in broad consensus among the participants.

On other ideas there was divergence. One of the more interesting divergent ideas concerned the most effective routes to developing organisms engineered for particular purposes. The routes are not mutually exclusive but the two basic methodologies consist of directed evolution on the one hand and bottom up construction of new genomes on the other. Both have had success; time will tell which proves more profitable.

VI. Major Points Addressed During Post-Workshop Email Discussion

The questions below (in paraphrased form) were posed in a post-workshop email discussion. The consensus answers given here are also paraphrased from responses received.

1. *What are the three biggest technical challenges in Engineering Biology?*

(a) Understanding cellular networks (from genomic information) and hierarchical relationships molecular to cell, organism, tissue. (See, in particular, presentations by Lee, Lauffenburger, Palsson and Keasling.) This is a challenge to data acquisition, modeling, and design in biological engineering. Also lack of scalable design strategies for reliable biological design.

(b) Creating actual knowledge out of massive amounts of data (Palsson); a need for data standardization and validation (Georgiou); a national lab-type effort for validation

and accessible maintenance of large databases for modern biology would be invaluable.

(c) New, more rapid tools for biological synthesis and characterization (Lee, Laderman, Keasling); lack of diversity and utility of existing biological parts (Smolke).

2. *What are the bases for these challenges?*

Lack of resources is the unanimous response; given time and resources, these challenges will be (are being) addressed. Sustained research funding, especially for larger-scale developmental efforts is needed. The regulatory and public policy environments will have major impact on addressing these challenges. Researchers in these fields must be aware of ethical, environmental, economic and legal issues.

3. *What will be the accomplishments and capabilities made available over the next five to ten years?*

The general feeling among the responses is divided between biomedicine (designer drugs and therapeutic systems, new biomimetic devices for high-throughput drug testing, new agents to treat infectious diseases, stem cell therapies, understanding human biology) and biological manufacturing (biobased production of fuels, chemicals, and materials, replacing fossil resources). New capabilities in environmental sensing and remediation are also anticipated. In five years, expect new biologically-derived fuels to become more prevalent. Ten years will see biomanufacturing of high-value commodity chemicals, and on a slightly longer time-scale, impacts on agriculture to increase yield, improve food supply and decrease negative environmental impacts. Synthetic biology will deliver more advanced solutions in health and medicine (e.g. genetically programmed regenerative medicine, or synthetic organs and tissues) and environmental remediation (e.g. rebuilding devastated environments and ecosystems).

4. *Which among these will have biggest DOD impact?*

Biomedicine and biological manufacturing are also thought to have the biggest impact on DOD. Infectious disease treatment, defense against biological weapons, and situational awareness are thought to be DOD motivators in biomedicine, while economic and national resource security would be the drivers of interest for biological manufacturing. As the global population moves toward ten billion, there will be increasing competition for resources, food, and water, all of which can be addressed in some measure by biological engineering.

5. *How would you staff a large new synthetic biology center?*

The researchers should be dedicated to making biology into a fast and predictable technology for global sustainability – food, energy, commodities, environmental reporters, and human health – new molecular- and cell-based therapies, infectious disease treatment. *In silico* biological design would be an essential skill. Focus on development and implementation of tools that will make the engineering of biological systems more scalable, faster, reliable, versatile and cheaper. Training of staff should be in quantitative biology, chemistry, medicine, computer science and several areas of molecular engineering.

6. *Explain synthetic biology to the President and why it is important to the country*.

Biology is the technology of this century, much as silicon was the technology of the last. It is an essential platform for advancing manufacturing and medicine through the redesign of cells and biological systems. A good discussion of the definition of synthetic biology is found in the December 2009 issue of *Nature Biotechnology* dedicated to the topic and containing definitions from 25 experts in the field of synthetic biology (http://blogs.nature.com/nautilus/2009/12/nature_biotechnology_focus_on.html).

A simple, true statement is that *synthetic biology re-engineers organisms to produce non-native products and perform non-native functions*. Synthetic biology, as a subfield of biological engineering, is the application of engineering principles to the design, construction, and characterization of biological systems. A central goal is to make the engineering of biology faster and more predictable, and thus to enable all constructive biotechnologies. Synthetic biology is disruptive, with the potential to transform biological engineering, which until now has been limited to tinkering with and around natural organisms, and relies on a good deal of serendipity for success.

Appendix: Workshop Program

Future Directions in Engineering Biology

April 4-5, 2011 | Berkeley, CA

I. Day 1: April 4, 2011, The Boiler Room Main Floor, Hotel Shattuck Plaza

8:30-9:00 am: Welcome and Charge

Graham Fleming, Vice Chancellor for Research, Department of Defense representatives, Adam Arkin, Matthew Tirrell

9:00 am-12:00 pm: Chemical Synthesis and Production, Adam Arkin, moderator

- *Discovery & Development of the Next Generation of Protein Therapeutics* -
  George Georgiou, Ph.D., Cockrell Family Regent's Chair in Engineering #9, Professor of Chemical Engineering and Biomedical Engineering, University of Texas at Austin
- *Engineering Microorganisms for Chemicals, Fuels and Materials* -
  Sang Yup Lee, Ph.D., Dean, College of Life Sciences and Bioengineering, Distinguished Professor of Chemical & Biomolecular Engineering, Bio and Brain Engineering, and Biological Sciences, Korea Advanced Institute of Science and Technology
- *Biological Engineering and Directed Evolution* -
  Willem 'Pim' Stemmer, Ph.D., CEO, Amunix, Inc.
- *Designing Sustainability* -
  Pamela Silver, Ph.D., Professor of Systems Biology, Harvard Medical School

12:00-1:00 pm: Lunch

1:00-3:30 pm: Biological Design and Assembly, Doug Clark, moderator

- *Engineering Biology and the Future of Bioanalytical Measurement* -
  Stephen Laderman, Ph.D., Director, Molecular Tools Laboratory, Agilent Research Laboratories
- *Gaining Access: Rebuilding Genetics from the Ground Up* -
  Christopher Voigt, Ph.D., Associate Professor of Pharmaceutical Chemistry, University of California, San Francisco
- *New Technologies in Genetic Manipulation of Salmonella to Develop Vaccines Against Infectious Diseases, Fertility and Cancer* -
  Roy Curtiss III, Ph.D., Professor of Life Sciences, Arizona State University
- *Biologically Inspired Engineering: Organs-on-Chips* -
  Donald Ingber, M.D., Ph.D., Director, Wyss Institute for Biologically Inspired Engineering, Harvard University; Judah Folkman Professor of Vascular Biology, Harvard Medical School &

Vascular Biology Program, Children's Hospital; Professor of Bioengineering, Harvard School of Engineering and Applied Sciences

3:30-4:00 pm: Break

3:30-5:30 pm: Biological Systems Modeling, Adam Arkin, Moderator

- *Modeling Biological Systems* -
  Douglas Lauffenburger, Ph.D., Ford Professor and Head of Biological Engineering, Professor of Chemical Engineering and Biology, Massachusetts Institute of Technology
- *Modeling Strategies for Drug Targeting and Biomarker Discovery* -
  Francis J. Doyle III, Ph.D., Mellichamp Chair in Process Control, Director, Institute for Collaborative Biotechnologies, Associate Dean for Research, College of Engineering, University of California, Santa Barbara
- *Biological Systems Modeling* -
  Bernhard Palsson, Ph.D., Galletti Professor of Bioengineering and Adjunct Professor of Medicine, University of California, San Diego

6:00-8:00 pm: Group Dinner – White Cotton Room 6th Floor, Hotel Shattuck Plaza

II. Day 2: April 5, 2011, The Boiler Room Main Floor, Shattuck Hotel Plaza

8:00-8:30 am: Energy, Agriculture, Environment and Other Applications, Doug Clark, moderator

- *Synthetic Biology for Synthetic Chemistry* -
  Jay Keasling, Ph.D., Professor of Chemical & Biomolecular Engineering and Bioengineering, University of California, Berkeley; CEO, Joint BioEnergy Institute; Associate Laboratory Director for Biosciences, Lawrence Berkeley National Laboratory

8:30 am-12:00 pm: Tissue Engineering and BioHybrid Systems, Matt Tirrell, moderator

- *Tissue Engineering from Bench to Bedside and Back* -
  Linda Griffith, Ph.D., Professor of Biological and Mechanical Engineering, Director, Biotechnology Process Engineering Center, Chair, Biological Engineering Undergraduate Programs Committee, Massachusetts Institute of Technology
- *Biopolymer Engineering for New Materials & Regenerative Medicine* -
  David Kaplan, Professor and Chair, Department of Biomedical Engineering, Professor of Chemical Engineering, Director, Bioengineering and Biotechnology Center, Tufts University
- *Engineering Molecular Devices*-
  Niles Pierce, Professor and Executive Officer, Department of Bioengineering, Professor of Applied & Computational Mathematics, California Institute of Technology

12:00-1:00 pm: Lunch

1:00-3:30 pm: Energy, Agriculture, Environment and Other Applications, Doug Clark, moderator

- *Biodegradation of Emerging and Conventional Water Contaminants* -
  Lisa Alvarez-Cohen, Ph.D., Fred and Claire Sauer Professor and Chair, Department of Civil and Environmental Engineering, University of California, Berkeley; Faculty Scientist, Ecology Department, Earth Sciences Division, Lawrence Berkeley National Laboratory
- *EcoDesign at an Event Horizon* -
  Gary Sayler, Ph.D., Professor and Director of the Center for Environmental Biotechnology, University of Tennessee, Knoxville
- *Synthetic Genetic Languages for Probing and Programming Cells* -
  Christina Smolke, Ph.D., Assistant Professor of Bioengineering, Stanford University
- *Synthetic Biology: Learning the Design Principles Cell Signaling Systems* -
  Wendell Lim, Professor of Cellular and Molecular Pharmacology, and Biochemistry and Biophysics, University of California, San Francisco

3:30-5:00 pm: General Discussion & Wrap Up

- Adam Arkin, Ph.D., Dean A. Richard Newton Professor of Bioengineering, University of California, Berkeley; Division Director, Physical Biosciences Division, Lawrence Berkeley National Laboratory
- Matthew Tirrell, Ph.D., Arnold and Barbara Silverman Professor and Chair, Department of Bioengineering, Professor of Materials Science & Engineering and Chemical & Biomolecular Engineering, University of California, Berkeley; Faculty Scientist, Materials Science Division, Lawrence Berkeley National Laboratory
- Douglas Clark, Executive Associate Dean, College of Chemistry, Professor of Chemical & Biomolecular Engineering, University of California, Berkeley

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